May 11, 2007

Mr. Michael E. Wall
Ms. Selena Kyle
Attorneys at Law
Natural Resources Defense Council
111 Sutter Street
San Francisco, California 94104

Dear Mr. Wall and Ms. Kyle:

This letter provides the Office of Environmental Health Hazard Assessment's (OEHHA) response to the Natural Resources Defense Council's (NRDC) June 6, 2006 petition asking OEHHA to administratively list 18 chemicals as causing reproductive toxicity under Proposition 65 (California Health and Safety Code section 25249.5 *et seq*.). The petition is based on entries in the National Institute for Occupational Safety and Health (NIOSH) "Pocket Guide to Chemical Hazards." NIOSH is an authoritative body, for purposes of Proposition 65. On December 15, 2006, in response to Carol Monahan-Cumming's letter of August 22, 2006, you submitted further information in support of the petition, providing additional rationales for listing the 18 chemicals identified in the Pocket Guide.

OEHHA has given very careful consideration to the petition and the additional supporting documentation you provided. We examined the documentation you provided in the context of the regulations governing addition of chemicals to the Proposition 65 list via the authoritative bodies mechanism, codified at Title 22, California Code of Regulations, section 12306. Further, we identified additional documents or sources of information, including those cited in the documentation you provided, that might provide support for listing chemicals via the authoritative bodies mechanism on the basis of a NIOSH or another authoritative body's document. Finally, we retrieved and reviewed the documentation relevant to the potential listing of three chemicals via the Labor Code provision of Proposition 65 (Health and Safety Code Section 25249.8(a)). We reached the following conclusions regarding the potential listing of the chemicals:

- Di-sec octyl phthalate, a synonym for DEHP (diethylhexyl phthalate), is already on the Proposition 65 list as causing reproductive toxicity.

- Hexafluoroacetone, nitrous oxide and vinyl cyclohexene diode may qualify for listing via the Labor Code provision of Proposition 65 (Health and Safety Code Section 25249.8(a)).

- Acrylamide is a candidate for administrative listing, based in part on a NIOSH criteria document and this process will proceed in due course. Acrylamide is listed as a carcinogen under Proposition 65.

- Carbaryl and p-nitrochlorobenzene may qualify for administrative listing based on NIOSH and other supporting documentation.

- Acetaldehyde and endosulfan may qualify for administrative listing based on U.S. Environmental Protection Agency and NIOSH documentation.

- It is unlikely the authoritative body listing criteria will be met for diphenylamine, formamide and styrene because the information provided by NIOSH as scientific references does not appear to meet the criteria for listing pursuant to Title 22, California Code of Regulations, section 12306(g):

    - For diphenylamine, no NIOSH documents are identified that could support listing. The *Registry of Toxic Effects of Chemical Substances* (RTECS) references an EPA Federal Register notice which concludes that "The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and/or postnatal exposure to diphenylamine. The reproduction study demonstrated that the offspring were less sensitive than the adults and there was no developmental toxicity observed in either the rat or rabbit developmental studies at any dose tested."
    - For formamide, one specific reference (Gleich, J. The influence of simple acid amides on fetal development of mice. Arch. Exp. Path. Pharmak. 228: Supl R25, 1974) is identified in the NIOSH Director's testimony to support the finding of positive teratogenicity in the mouse. This document is a one-paragraph abstract that does not meet the criteria of Title 22, California Code of Regulations, section 12306(g).
    - For styrene, the 1983 NIOSH document, "*Criteria for a Recommended Standard… Occupational Exposure to Styrene,"* under the section "Recommendations for a Styrene Standard," says, "Although the evidence is not strong, exposure to styrene has also been implicated with other adverse health effects such as … teratogenicity, and carcinogenicity. These health effects need further investigation, and would provide additional evidence for a reduction in the current occupational exposure standard if they were found to be styrene related." Thus, this document does not appear to provide sufficient scientific support for a formal identification of styrene as causing reproductive toxicity. In addition, with

regard to reproductive effects, the summary for styrene in the 1988 NIOSH Director's testimony states that for teratogenicity, styrene is "negative (in animal studies – limited human data inconclusive)."

- Monocrotophos and methoxyflurane are no longer used in the U.S. and there is unlikely to be any significant exposure to them. Monocrotophos, a food crop pesticide, is no longer produced here or elsewhere and tolerances for foods grown in or imported into U.S. have been canceled at the request of the pesticide producer. Methoxyflurane, an anesthetic gas, has been withdrawn for sale in the U.S. because of nephrotoxicity and hepatotoxicity. There appears to be little value in using OEHHA's limited resources to list these chemicals under these circumstances.

- Diethyl phthalate, 1,2,4-trichlorobenzene, diaminoanisole and trimethyl phosphite do not appear to meet the administrative listing criteria because the RTECS does not provide adequate scientific basis for listing pursuant to Title 22, California Code of Regulations, section 12306(g), and no other basis for listing was identified. A disclaimer at the beginning of the RTECS file for each chemical reads "NOTE: TOXICITY DATA HAVE NOT BEEN EVALUATED." This sentence makes the scientific basis for NIOSH's conclusion about reproductive toxicity unclear. However, since there are some data indicative of reproductive toxicity for these four chemicals, OEHHA has entered them into its tracking data base. They will be prioritized in accordance with OEHHA's December 2004 document "*Process for Prioritizing Chemicals for Consideration under Proposition 65 by the 'State's Qualified Experts*." The data that are indicative of reproductive toxicity are as follows:

    - For diethyl phthalate, the NIOSH Recommended Exposure Limit, or REL, is based on "smaller than normal fetuses in animals." A NIOSH 1995 document supporting the REL gives a basis for the REL and identifies RTECS and the Hazardous Substances Data Base as the references for the reproductive effects. RTECS lists a number of studies indicating that multiple species and routes were tested and found reproductive effects.
    - For 1,2,4-trichlorobenzene, the Pocket Guide refers to "possible teratogenic effects" as symptoms and the reproductive system as the target organ, citing RTECS. RTECS lists two studies for reproductive effects.
    - For diaminoanisole, the Pocket Guide lists "teratogenic effects" as symptoms and "reproductive system" as the target organ. RTECS indicates one subcutaneous study with preimplantation loss, and also refers to the NIOSH Compendium, which identifies a Current Intelligence Bulletin (CIB) from 1978. The CIB mentions cancers of the reproductive system, but does not mention reproductive toxicity.

- For trimethyl phosphite, the Pocket guide lists as a symptom "in animals: teratogenic" and as a target organ the reproductive system. RTECS refers to a single study and to the NIOSH Compendium, which identifies no supporting documentation on trimethyl phosphite but does mention "teratogenic and reproductive effects in animals" under health effects in the summary table.

Based upon these findings, as time and resources allow, OEHHA will pursue the appropriate listing process for those chemicals that appear to meet the criteria for administrative listing noted above. We appreciate the concern you hold for the public health and your interest in Proposition 65. If you have any questions, I can be reached at (916) 322-6325.

Sincerely,

[Original signed by]

Joan E. Denton, Ph.D.
Director